

CLAIMS

1. A method of protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or  
5 from either to a type II diabetic state, which comprises administering to the subject a protective amount of at least one agent which is

(1) a polypeptide which is substantially structurally identical  
10 or conservatively identical in sequence to a reference protein which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtables 1A and 1C, or (b) selected from the group consisting of human proteins within at least one of the human protein classes set forth in  
15 master table 2, subtables 2A and 2C,

or

(2) an expression vector encoding the polypeptide of (1) above  
20 and expressible in a human cell, under conditions conducive to expression of the polypeptide of (1);

where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from  
25 either to a type II diabetic state.

2. A method of protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from  
either to a type II diabetic state which comprises administering  
30 to the subject a protective amount of at least one agent which is

(1) an antagonist of a polypeptide, occurring in said subject, which is substantially structurally identical or conservatively  
35 identical in sequence to a reference protein which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B and 1C, or (b) selected from the group consisting of human proteins belonging to at

least one of the human protein classes set forth in master table 2, subtables 2B and 2C,

(2) an anti-sense vector which inhibits expression of said polypeptide in said subject,

where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

3. A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of at least one "favorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtables 1A and 1C, or (b) selected from the group consisting of human proteins within at least one of the human protein classes set forth in master table 2, subtables 2A and 2C,

and directly correlating the level of expression of said marker gene with the propensity to progression in said patient.

4. A method of screening for human subjects who have a propensity for progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of at least one "unfavorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is (a) selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B and 1C, or (b) selected from the group consisting

of human proteins belonging to at least one of the human protein classes set forth in master table 2, subtables 2B and 2C,

and inversely correlating the level of expression of said marker gene with the propensity to progression in said patient.

5 5. The method of claims 1 or 3 in which the reference protein is of subtable 1A or of a class set forth in subtable 2A.

10 6. The method of claims 1 or 3 in which the reference protein is of subtable 1B or of a class set forth in subtable 2B.

7. The method of any one of claims 1-6 in which (a) applies.

15 8. The method of any one of claims 1-7 in which the reference protein is a human protein.

9. The method of any one of claims 1-7 in which the reference protein is a mouse protein.

20 10. The method of any one of claims 3 or 4 in which the level of expression of the marker protein is ascertained by measuring the level of the corresponding messenger RNA.

25 11. The method of any one of claims 3 or 4 in which the level of expression is ascertained by measuring the level of a protein encoded by said marker gene.

30 12. The method of any one of claims 1-9 in which said polypeptide is at least 80% identical or at least highly conservatively identical to said reference protein.

13. The method of any one of claims 1-10 in which said polypeptide is at least 90% identical to said reference protein.

35 14. The method of any one of claims 1-11 in which said polypeptide is identical to said reference protein.

15. The method of any one of claims 1-14 in which the E-value cited for the reference protein in Master Table 1 is not more

than  $e^{-6}$ .

16. The method of claim 15 in which the E-value cited for the reference protein in Master Table 1 is less than  $e^{-10}$ .

17. The method of claim 17 in which the E value calculated by BLASTN or BLASTX would be less than  $e^{-15}$ , more preferably less than  $e^{-20}$ , still more preferably less than  $e^{-40}$ , even more preferably less than  $e^{-60}$ , considerably more preferably less than  $e^{-80}$ , and most preferably less than  $e^{-100}$ .

18. The method of any of claims 2-17 in which the antagonist is an antibody, or an antigen-specific binding fragment of an antibody.

19. The method of any of claims 2-17 in which the antagonist is a peptide, peptoid, nucleic acid, or peptide nucleic acid oligomer.

20. The method of any of claims 2-17 in which the antagonist is an organic molecule with a molecular weight of less than 500 daltons.

21. The method of claim 20 in which said organic molecule is identifiable as a molecule which binds said polypeptide by screening a combinatorial library.